OSSEOUS PLAQUES OF THE PIA-ARACHNOID AND THEIR RELATION TO PAIN IN AKROMEGALY.

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Since Marie in 1886 first named and described the symptom-complex known as akromegaly, many and numerous have been the observations reported. The pathological findings as well as the symptoms have varied. The major clinical features, such as increase in size of the extremities, nose, lips and lower jaw, however, we now consider as distinctive.

Among the lesser symptoms, pain seems to play an important role. It was Sainton and State (1) who first called attention to its prominence. In analyzing the cases in literature, they found it present in 50 per cent. of the cases. Sousa Leita (2), Sternberg (3) and others considered it for the most part as a transient symptom. Osborne (4) believes that almost every case of akromegaly has pain more or less constant in some portion of the body, but he included head pains.

As to the pathology of these pains, Sainton and State believe them to be due to the presence of osseous plaques in the spinal pia and to the changes, mechanical and irritative, caused by them upon the nerve roots and substance of the cord. This I do not believe to be correct, and it is the object of this article to show that there is no definite pathology of the spinal cord in akromegaly, and also to show that these plaques play little or no part in the production of the pain of this disease.

The pains referred to by Sainton and State were distributed sometimes in the extremities, sometimes in the spinal column, and sometimes in the joints. They divided them into five classes—osteo-arthritic, neuralgic, muscular tabetic and akro-paresthetic. The findings in the case they report include the osseous plaques in the spinal cord together with degenerations of Goll's tract and Gowers' tract. The role of these plaques they suggest, is probably mechanical, and they cite the similar findings in cases reported by Duscheneau, Henriot, Finzi and others.

To observe whether mechanical pressure exerted any influence I examined several nerves lying under these plaques and found no evidence of thickening or any degenerative change. The spinal cord in two cases, examined in the lumbar and cervical regions, showed only a slight increase of the neuroglia, and the presence of arteriosclerosis; this latter accounting for the neuroglia increase. Other cases in literature showed a similar picture. A review of the pathological findings, as collected by Sternberg (5), Hinsdale (6), Brooks (7), Arnold (8) and others shows that changes in the spinal cord are inconstant, the cord being normal in many cases—Packard (9), Cagnetto (10), Strümpell (11), etc.; in other instances showing varying degenerations of the tracts—Sainton and State (12), Adler (13), Cagnetto, Arnold; in others syringomyelia, and in Barrett's (14) case the picture of a severe anemia. In the case I report only arteriosclerosis was to be noted.

Furthermore, plaques are very frequently present in many diseased states and in conditions in which no pain is present. Virchow (15) long ago emphasized this. "For a long time," he says, "they were thought to be the cause of tetanus, chorea and all other forms in which pain was a prominent symptom." They reasoned that the presence of the bone and its processes caused a strong irritation of the nervous system. "This is an error because we frequently find them present in individuals who have not the slightest symptoms."

Zanda (16) was able to collect sixty-three cases showing osseous plaques and found that half occurred in mental disease, that they were frequent in retrogressive changes, as old age, chronic insanities, diseases of the spinal cord, tuberculosis, marasmus and chronic suppuration.

The giant, Wilkins, reported by Bassoe (17), gave no history of pain throughout his life and yet many thickened, partly calcified plaques were found, one even adherent to a nerve root. Microscopically, there was a moderate amount of diffuse degeneration of the spinal cord. Linsmayer's (18) case of akromegaly showed osseous plaques with no definite microscopical changes in the spinal cord or nerve roots save arteriosclerosis and clinically there were no symptoms of pain. Strümpell's (19) and Cagnetto's (20) cases showed a similar picture. In the case reported by

Pearce Bailey (21) pain was a prominent symptom in the hands and feet, radiating to the shoulder and to the hips; yet the spinal cord, grossly, showed no changes, and microscopically showed only thickening of the arteries. In Packard's (22) case, sections of which I have studied, the pains were only present during the period of onset, a duration of three to five years. Since that period the patient had been free from pain. The examination of the spinal cord by Dr. Spiller (23) showed grossly numerous plaques, and microscopically no degenerations.

It seems to me that we must look elsewhere for the explanation of these pains. In reviewing the pathological findings of these cases of akromegaly, the prominent feature of arteriosclerosis should be noted, and the trophic changes incident thereto, in the joints, muscles, viscera, skin and spinal cord could easily explain this symptom. In the arthritic pains the excessive production of lime salts, dependent upon arteriosclerosis and also upon the retention of lime salts and phosphorus in akromegaly, as shown by Moraczewski (24), explains the pathology of pain in the joints.

Arnold (25) and Cagnetto (26) and others have examined the muscle and have shown the presence of connective tissue overgrowth and degeneration of the muscle substance itself. The presence of a chronic myositis here might easily explain the incident of muscle pains in any period of the disease.

The question as to the origin of these plaques is of some interest. Virchow (27) long ago thought them direct transformations of connective tissue into bone. Rokitansky (28), Ziegler (29), Schmaus (30) simply mention their frequency in the pia-arachnoid and describe their gross appearance. Zanda (31) has found that the bone formation takes place from the dura after adhesion with the arachnoid is formed. In the cartilaginous period they have no connection with the dura. In the stage of ossification, blood vessels from the dura grow into them. Their frequent presence in retrogressive conditions, such as senility, uremia, mental disturbances, in fact, in all those conditions in which arteriosclerosis is associated or plays a leading part, indicates clearly to me the natural overgrowth of connective tissue from passive congestion and chronic irritation, and in such areas of connective tissue overgrowth lime salts are frequently deposited. Among the favorable situations for this process are the blood vessels, lymph nodes, lungs and spinal cord. The associated finding of arteriosclerosis in many cases of akromegaly indicates clearly one of the predisposing factors for the production of osseous plaques.

The first case I wish to report shows the presence of these osseous plaques in uremia and arterio-capillary fibrosis. The clinical history of this case unfortunately is very meagre. The patient, D. B., an old man, was brought to the Philadelphia General Hospital in an unconscious condition. He lived three days. The physical examination by Dr. Potts showed no paralysis of face or extremities. The diagnosis of uremia and chronic interstitial nephritis was made and was corroborated at the necropsy. General atheroma of the cardio-vascular system was also noted, together with chronic endocarditis. Examination of the spinal cord showed numerous plaques covering the posterior surface from the cervical region to the lumbar. These measured from 1 to 3 cm. and were cartilaginous in appearance; a few had the firmness of bone.

Microscopical Examination.—Transverse and longitudinal sections were made of these plaques, and stained with eosin-hematoxylin. Those cut transversely show a central zone of osteoid material; surrounding this are layers of fibrous tissue, hyaline in character. In this are to be noted a few cells, resembling osteoblasts. The upper surface of the section shows only a few connective tissue cells; the lower shows a more active proliferation of connective tissue. In this region the plaque was in contact with the substance of the cord. This proliferation occurs in the pia. No evidence of true bone is to be seen.

The spinal cord was studied with Weigert, hemalum and Nissl stains. A moderate increase of neuroglia in certain parts of the column of Goll of the cervical section and arteriosclerosis are the chief features noted. In the lumbar region the arteriosclerosis is not so marked. There is marked thickening of the spinal pia throughout.

A study of the spinal nerve roots under these plaques showed no evidence of mechanical pressure. No changes were to be noted by the Weigert or hemalum stains.

In the second case, one of akromegaly, the clinical features reported by Dr. Packard in the *American Journal of Medical Sciences*, 1892, and by Dr. Spiller pathologically before the Philadelphia Neurological Society, showed these plaques grossly. Microscopically, by the Weigert, hemalum and Marchi's method no evidences of degeneration were to be noted.

The clinical notes by Dr. Packard, 1892, may be briefly summarized. Patient was first seen in 1885. In 1877 had pains all through his body, which were supposed to be rheumatic. Since that time until 1885 had vague pains through his body with gradually increasing weakness of the legs. In 1892 he was again examined. Aside from headache no other symptoms of pain were noted. Temperature, pain and tactile sensations in the extremities were good. Knee jerks were absent. His general health was farly good. Beside the distinctive features of akromegaly no other symptoms relating to the subject are to be noted.

Examination of the cord in the lumbar and sacral regions failed to show any degeneration.

To summarize briefly:

1. Osseous plaques are frequently present in the pia-arachnoid.
2. They are found in many diseases, such as uremia, tuberculosis, retogressive conditions, etc.
3. Arteriosclerosis seems to be the underlying factor in their causation.
4. The presence of these plaques upon the spinal pia in akromegaly does not explain the production of pain in that disease.
5. There is no definite pathology of the spinal cord in akromegaly.

I wish to thank Dr. Spiller, under whose direction this work was undertaken, for the privilege of reporting these cases, and for his assistance in the examination of the material.

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